Stable vs. Silent progressive Multiple Sclerosis: A real world retrospective clinical imaging Brazilian study

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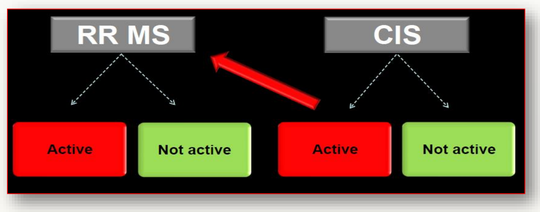
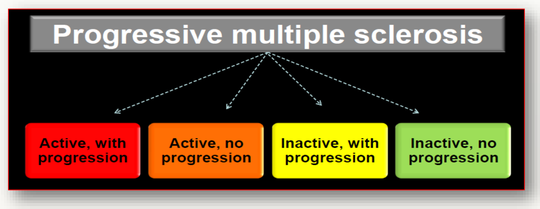
Background. **New MS phenotypes propose clinical and imaging requirements to characterize activity and progression in MS patients[1]. Clinical relapses and MRI findings are established markers of disease activity, but progression parameters remain far from clear cut characterization. No evidence of disease activity (NEDA), an ideal target for long term treatment, includes neither clinical nor imaging signs of disease (NEDA 3), a concept stringently enriched by the inclusion of brain atrophy measurements (NEDA 4).**

New times, new phenotypes…



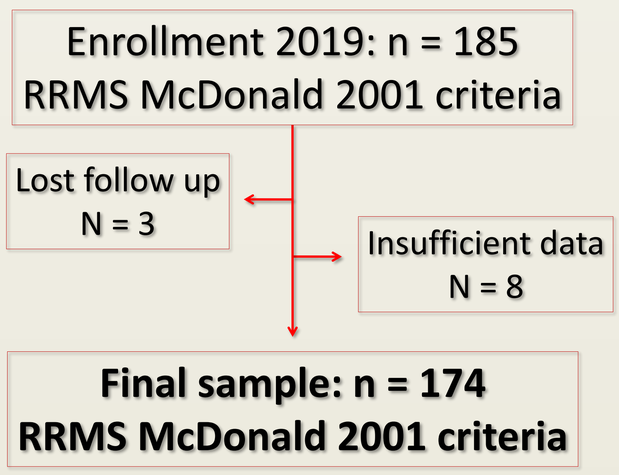


	Current markers
Activity	Clinical: relapses
	MRI: Gd+ or new/enlarging T2W
Progression	Clinical: increasing dysfunction/disability (EDSS)
	MRI: not yet established*

** "Under consideration are increasing number and volume of T1W hypointense lesions, brain volume loss,…MTR and DTI".*

Our team did a retrospective open label study comparing clinical and imaging data between apparently stable relapsing remitting MS patients over last 7 years and its impact on present concepts of disease phenotypes.

Design and Method. **Data from 185 consecutive non selected patients with diagnosis of relapsing remitting MS (McDonald 2001), admitted from 2001 to 2012 on our Treatment Program were included. Accepted patients had at least 3 MRI available studies with proper protocol leading to a reliable evaluation of activity and progression over the last 7 years. Eleven patients were excluded: 3 cases for lost follow up and 8 for insufficient data. Annual clinical evaluation included relapses and EDSS evolution, for at least 7 years (mean 8.4). MRI data included the presence of gadolinium enhancing lesions or new/enlarging T2W lesion as well as the annualized evolution of corpus callosum index (CCI)[2] (figure 1).**



CCI is a simple and feasible method for a two-dimensional measure of corpus callosum using an orthogonal semi-automated linear model applied on a conventional mid-sagital T1W imaging. Normalized CCI showed a good intra and inter rated observers correlation as well as with brain parenchymal fraction, EDSS and PASAT scores [2,3,4,5].

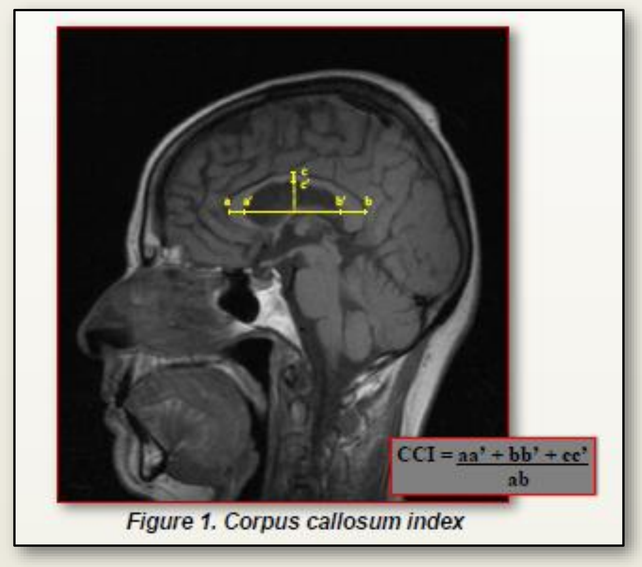
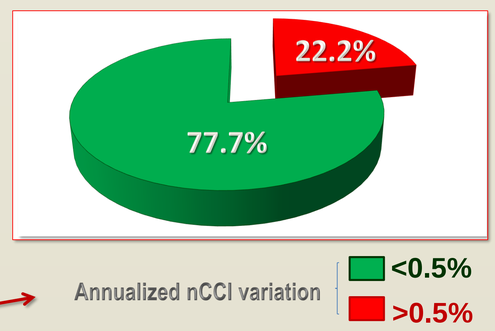


Figure 1. Corpus callosum index

Results. **After a minimum of 7 years follow up, from 174 patients of the original sample 148 showed no confirmed progression on EDSS and were considered the "clinically stable" group (table 1), and 33 patients (22.2%) showed an annualized reduction on normalized CCI (nCCI) of more than 0.5%, cut off for a significant brain atrophy score (table 2).**

N = 148	
Mean age (range)	36.6 (17-61)
Male/Female	62/86
Years of disease (mean)	8.4 (3.7-11.7)
Mean EDSS (range)	3.7 (1-5.5)
ARR	0.21
Mean T2W lesions (range)	7.3 (4-17)
Annualized nCCI (range)	0.331 (0.28-0.583)

Table 1. Demographic data of "stable group"



N = 115 (77.7%)	N = 33 (22.2%)
32.4 (17 - 44)	37.3 (27 - 61)
44/71 *	18/15 *
6.3 (3.7-8.8) **	8.6 (7.1-11.7) **
3.1 (1-4)	3.9 (2.5-5.5)
0.18	0.22
5.2 (4-9)	8.7 (6-17)
0.317 (0.28-0.433) **	0.361 (0.308-0.583) **

Table 2. Comparative data of subpopulations

** p< 0.001*
*** P< 0.01*

Conclusions. **From a population of 148 apparently "stable" MS patients over at least 7 years follow up period, 1/5 of them showed significant progressive brain atrophy.**

More robust data are required but it seems reasonable to conclude that routine brain volumetry can provide valuable information about the real state of treatment response, potentially selecting these "silent progressive" [6] patients for a switch to a more aggressive therapeutic strategy.

The authors have no conflict of interests in this paper to disclose.

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